

Björn E. Rydberg, Ph.D. In Memoriam

With great sadness we report that LBNL Staff Scientist Björn Rydberg passed away unexpectedly on December 11, 2011, at the age of 68. Dr. Rydberg, who was born in Sweden and received his Ph.D. in biophysics from Uppsala University, had been with the Life Sciences Division since 1990. He was internationally recognized as an expert in radiation-induced DNA strand breakage and rejoining, with special expertise in effects of high-LET particles such as those in galactic cosmic rays. He published more than 55 scientific papers and was an outstanding experimentalist with a deeply analytical approach to understanding the effects of ionizing radiation on mammalian cells. His passing is a profound loss for the radiation research community.

Björn had a remarkable career in the field of DNA damage and repair. His strong conceptual understanding of DNA structure and of radiation physics, combined with his gifts in assay development and experimental design, gave him a special perspective on this field and a unique ability to address pivotal questions. His love for charged particle research was undeniable.

Born in Sweden on May 31, 1943, Björn earned his BA in Engineering Physics from the Royal Institute of Technology, Stockholm in 1966, and then worked at the Swedish Research Institute of National Defense, where he published two papers in nuclear physics [1, 2]. He went on to obtain his Ph.D. in Biophysics from Uppsala University in 1975. His Ph.D. degree was awarded for his analysis of radiation-induced DNA strand breakage in mammalian cells using the alkaline unwinding DNA strand separation assay [3]. Soon after Björn began using the alkaline unwinding assay, he published what is still regarded as a brilliant analysis of the theoretical basis of this technique [4]. He also immediately recognized that his assay could be used to study replication forks in mammalian cells, with the nicks between 'Okazaki' fragments serving as starting points for unwinding in alkali [5]. During his postdoctoral training at Yale University from 1975 to 1977, Björn used the same technique to detect radiation-induced DNA strand breaks and their rejoining in crypt cells of the small intestine of the mouse [6, 7]. Upon completing his postdoc, Björn went back to Sweden to take a position at the Swedish Research Institute of National Defense, where he worked from 1977 to 1980. His work there expanded to include the study of mismatch repair in *E. coli*, published as a series of three single-author papers [8-10]. Also during this period, Björn became a docent for physical biology at Uppsala University, where he lectured until 1984. In 1980, he began a collaboration with Tomas Lindahl's group, then at the University of Gothenburg, in which he identified the mutagenic potential of non-enzymatic DNA methylation by S-adenosyl-L-methionine [11]. Clearly ahead of his time, he also further refined the alkaline unwinding technique, improving the assay's sensitivity [12] and allowing for high-throughput analysis with cell cycle specificity using fluorescent probes and flow cytometry [13]. In 1983, while on leave from Uppsala University, Björn worked with Gerhard Kraft's group at the Gesellschaft für Schwerionenforschung in Darmstadt, Germany, where he developed his interest in high Linear Energy Transfer (LET) radiation and radiation quality effects. In 1987 he joined the Clare Hall Laboratories in the UK, where with Peter Karran he focused his efforts on cloning and chromosomally mapping the human O⁶-methylguanine-DNA methyltransferase gene [14, 15], a gene encoding a methyl-acceptor protein that removes carcinogenic, methylated lesions from the DNA.

In 1990 Björn joined LBNL, first working with Bea Singer to identify novel enzymatic activities of a DNA glycosylase in the base excision repair pathway [16, 17]. He then joined the radiation biophysics program at LBNL and the groups of Priscilla Cooper and Aloke Chatterjee, taking advantage of an interdisciplinary research environment that thrived, in large part, due to his active involvement. It was during this period that Björn returned to his earlier interests in the unique properties of charged particle radiations and their interaction with DNA. Papers of particular importance in the field of high-LET radiation effects include a quantitative comparison of double-strand break (DSB) yield for X-rays versus high-LET radiation using pulsed-field gel electrophoresis (PFGE). These studies revealed unexpectedly that Relative Biological Effectiveness (RBE) levels calculated from DSB data were considerably smaller than from parallel experiments using survival as an endpoint, and actually lower than 1.0 [18, 19]. This paradox was largely resolved by Björn's experiments using a carefully conducted new experimental

approach that he designed to allow the detection of small, previously unrecognized fragments of DNA from human fibroblasts exposed to accelerated nitrogen or iron ions (LET range from 97-440 keV/ μ m) [20, 21]. Using this advanced analysis method to correct the DSB yield by inclusion of DNA fragments below 200 kilobase pairs (kbp), the corrected RBE values for DSBs were significantly greater than previously reported, matching more closely those obtained for cell survival and also being in much closer agreement with theoretical calculations performed by Bill Holley and Alope Chatterjee. In related work, calculations by Holley and Chatterjee based on the 30-nm solenoidal chromatin fiber had predicted that the distribution of DNA fragment lengths induced by charged particles should be highly dependent on the approximate symmetries of the chromatin structure. Indeed, the theoretically predicted small DNA fragments of 78-450 bp were detected by Björn, and his measurements of the discrete size classes of fragments formed allowed the team to discriminate between two proposed models for the structure of chromatin [22, 23].

Studies performed with Markus Löbrich that were initiated while Markus was a postdoc at LBNL were also extremely important in elucidating the basis for the high biological effectiveness of high-LET radiation. Together they developed an assay that combined PFGE separation of rare-cutting restriction fragments from DNA of irradiated mammalian cells with detection of intact fragments by hybridization to allow, for the first time, analysis of the fraction of correctly vs. incorrectly rejoined DSBs after exposure to different radiation qualities [24]. Using this assay, Björn found that the mis-rejoining frequency for X-rays was non-linear and increased significantly with dose, in keeping with cytogenetic data. In contrast, the dose dependence for mis-rejoining with high LET particles was closer to linear, with mis-rejoining frequencies that were much higher than for X-rays, particularly at more biologically relevant lower doses [25].

Björn's background in engineering physics gave him a unique ability to understand the beamline physics at the Berkeley BEVALAC and the 88-inch cyclotron, as well as the Brookhaven synchrotron, where he worked closely with the physicists to tailor the beamline to achieve the biological objectives. During his extensive work on NASA-funded projects he mentored many students and postdoctoral fellows, often informally, to help them understand how to design good experiments at accelerators, how best to implement them, and how to interpret the results. It was evident that many individuals from institutions around the world thought very highly of Björn and were impressed by his creativity and attention to detail, especially the beamline physicists at BNL who were delighted to have him there to do experiments again in the recent Fall 2011 run. It was an honor for his LBNL Life Sciences colleagues with NASA-funded projects to be there working with Björn. Yet, when anyone mentioned the obvious esteem in which he was held at BNL, he replied in his typical modest way "well, I've been around for some time".

Björn was a highly versatile scientist, drawing on approaches from diverse disciplines including molecular biology, biochemistry, and cytogenetics. His superb experimental work was regularly accompanied by brilliant mathematical analyses of the theoretical basis of the methods used. The rigor of his science and the inordinate care he took to avoid over-interpreting his findings were among the reasons he was held in such high regard by colleagues around the world.

As a mentor, Björn was a unique and cherished individual. He always had an open door, never made anyone feel less for asking, and took the time to explain complicated topics. He frequently would greet visitors to his office with a slight grin, as if he were expecting them, or knew something they didn't (which was often the case!). He was not a big talker, but when he did say something, everyone knew it was worth listening. Björn radiated a calm that made it nearly impossible to get too frustrated about a failed experiment or when things didn't work out as planned. He also had a wonderful sense of humor that often surprised people who were lucky enough to see the fun-loving side of him. He was quite athletic, bicycling to and from work each day between his home in Albany and his laboratory at the Potter Street campus (Building 977).

Björn's passing is a profound loss for the scientific community. He was a valued colleague, mentor, and friend to many in Life Sciences, and he was the devoted father of Ilari and Ulrika Rydberg and loving husband of Leena Rydberg. His intelligence, quiet presence, warm demeanor, and gentle smile will be sorely missed in the halls of LBNL and at the NASA Space Radiation Laboratory at BNL.

A private memorial service was held on December 29, 2011.

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